

THE HISTORIC EVOLUTION OF VARIOLATION.

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THE HISTORIC EVOLUTION OF VARIOLATION.* †

By ARNOLD C. KLEBS, M. D., Lausanne, Switzerland.

Immunology, the latest child of medical science, has reached, [69] after a short existence, a very considerable development, some even think maturity. However true this may be, its creation has certainly called forth efforts of the most varied nature embracing and mobilizing almost all branches of physical sciences. The very acuteness of these efforts is inimical to retrospection. Only very recently some experimenters have searched the earlier literature, of vaccination for instance,¹ for support of their conception. Variolation has entered very little, if at all, into such investigations and it is really astonishing how thoroughly it is forgotten, this most interesting epoch in medical history, which kept greater and humbler minds in fever heat during almost one whole century. This oblivion is particularly curious because variolation called forth a unique and extensive trial of a specific preventive method, the logical consequence of which was vaccination. This fact does not detract from the merits of Jenner, who by observation and conclusive experiment was enabled to render an immortal service. It is true that Jenner was unaware of the generic identity of vaccinia and variola, that to him cowpox was a disease *sui generis*, the inoculation of which conferred im-

* Authors in 18th century literature speak only of "inoculation" (ingrafting, insertion). At present for the sake of clearness the term "variolation" seems preferable. In retrospective reviews of the subject the term vaccination is often used erroneously for variolation and a similar confusion is likely to occur if modern writers persist in using faultily the words "vaccine and vaccination" for protective and therapeutic inoculation generally.

† Paper read before The Johns Hopkins Hospital Historical Club, October 14, 1912.

¹ von Pirquet, *op. cit.*, introduction.

[69] munity to smallpox for some unknown mysterious reason. It is this conception which stamped vaccination as a new departure and it is largely responsible for the oblivion into which variolation has fallen. Jenner's belief² in the common derivation of cowpox and smallpox from the grease of horses, and Pearson's and Baron's vague suspicions of a more intimate relationship between variola and vaccinia, passed unnoticed for almost another century, after which the intrinsic analogy of variolation and vaccination could be demonstrated.

In searching for the earliest origins of variolation I may cite the words of Sir George Baker,³ one of the most scientific inoculators of his time: "It cannot but be acknowledged that the art of Medicine has, in several instances, been greatly indebted to accident and that some of its most valuable improvements have been received from the hands of Ignorance and Barbarism." This indebtedness to the intuitive genius of popular reason and procedure is strikingly illustrated in the reports of early practice of variolation. While the learned since oldest times strained every effort towards the discovery of a Medicinal antidote, the simple-minded evolved the idea of protective inoculation. It is difficult to ascertain any one locality where variolation was first practised. From its wide distribution it would seem that it arose spontaneously in various places where the need for it occurred. The earliest alleged reference to variolation in the chronicles of the 6th century by Marius, Bishop of Avenches, I have been unable to verify.⁴ I found only the well known report of a deadly [70] epidemic (570 and 571 A. D.) in Italy and Gaul of a disease which for the first time is called "variola."⁵ Clearly referring to variolation is a remarkable verse of the School of Salerno⁶

² Jenner, Inquiry, 1798, 3d paragraph.

³ G. Baker, An inquiry, etc., 1766, p. 1.

⁴ Edit. Bouquet, Histoire des Gaules, II, 12.

⁵ Smallpox is hereby not defined with any certainty. Its root *varus* as used by Celsus and Pliny is meant to indicate a pustulous disease, especially of the face.

⁶ S. de Renzi, *Flos Medicinae Scholae Salerni*, Naples 1859, p. 90 (3059, *et seq.*). A footnote of the editor gives as his opinion that the first two lines refer to variolation, which was not invented in the 18th century, or in Greece, but is older.

(10th or 11th century) entitled *adversus variola* and which [70] runs as follows:

*Ne pariant teneris variolae funera natis
Illorum venis variolas mitte salubres.
Seu potius morbi contagia tangere vident
Aegrum aegrique halitus, velamina, linteas, vestes
Ipseque quae tetigit male pura corpora dextra.⁷*

For preventive purposes the voluntary transference of a benign variola is surely recommended here, the *venis*, however, may indicate "system" generally, in which case the disease is to be transmitted by simple exposure or we may take it more literally and an operation then suggests itself. The last three lines giving preference in very modern-sounding language to the avoidance of infection by contact, seems to me to lend strength to the latter interpretation.

The first authentic reports of this practice we find in the Ephemerides of the Academia Cæsarea Leopoldino-Carolina published at Leipzig between 1670 and 1705. Here Dr. Vollgnad of Breslau⁸ in 1671 and Dr. Schultz of Thorn in 1677 clearly report instances of the custom of "buying the smallpox." There is, however, no reference made to the actual inoculation with the pock scabs purchased in the plague house, but that such was done is very likely, since Schultz speaks of the rather serious illness which his own brother acquired in this manner. It does not seem to me that these cases have anything to do with the sympathetic transference of disease, which agitated some medical minds of the day, and as instances of which they obviously were reported. Creighton⁹ gives an interesting example of this form of transplantation in 1657: "Some persons in the smallpox keep a sheep or a wether beside them in the chamber, those animals being

⁷ This may be rendered: In order that variola may not produce death among tender babes, put into their veins a favorable variola. Better still they should avoid touching the contagium of the disease: the sick person, the breath of the sick, the clothes, the coverings, the garments and such clean bodies as he may have infected (*tetigit male*) with his hand.

⁸ H. Vollgnad (1634-1682), member of Academy, 1669.

⁹ Slatholm (Buntingford), 1657, cited in Creighton, History of Epidemics in Britain, p. 475.

[70] apt to receive the envenomed matter and draw it to themselves"—only a slight modification of the Jewish scape-goat! Of course this has as little to do with variolation as the Biblical passage cited by Massey in 1722 in condemnation of inoculation: "So went Satan forth from the presence of the Lord and smote Job with sore boils from the soles of his feet unto his crown" (Job, II, 7).

Further reports of the ancient practice all date from the time of the medical introduction of variolation to Europe and America. They were of the usual order, meant to show that there is nothing new under the sun and some of them, therefore, have to be taken with caution. Thus we hear of a crude variolation in Scotland (Monro I., & Kennedy), in Wales (Perrot Williams),¹⁰ in Auvergne and Perigord (de la Condamine), in Jutland (Bartholin), in the Duchy of Cleve (Schwencke) and other parts of Germany. Of the inoculations practised in Greece, whence it was introduced to Western Europe by way of Constantinople, I shall speak later. The earliest traces of variolation are found in Asia and in Africa. In Africa the practice continues to this day among certain tribes, chiefly negroes, in the eastern, central and western regions. On the White Nile in the equatorial province (Welson & Felkin) among the Bari, and further east among the Somali (Stahlmann) a similar custom is found. It seems to have been highly developed by the most important of the native Bantu tribes, the Baganda, living northwest of Lake Victoria in the old Kingdom of Uganda. Further west we find the Wanjamwesi, and in the Sudan the Ashanti, and some Moorish tribes practice inoculation on their children. From northern Africa we have the report of the Tripolitan Ambassador, Kassem Aga, which made the round of 18th century literature, about the ancient variolation by Mohammedan tribes in Tripolis, Tunis and the Kabyl mountains. Not long ago we had a verification of this latter report by a French naval physician, Dr. H. Gros,¹¹ stationed at Rébéval in Algeria. He has observed a considerable number of variolations practised by Arabs and Kabyles and curiously enough

¹⁰ *Philos. Transact.*, 1722.

¹¹ *La variolisation*, *Janus*, 1902, VII, 169.

comes to the conclusion that variolation ought to be resorted [70] to if, for some reason or other, the supply of vaccine became exhausted. This account contains many interesting observations which corroborate most of the historical records of the 18th century.¹²

Exceedingly interesting accounts about smallpox inoculations are available from Asia. I can only briefly refer to them. China, of course, again is said to have known variolation since remotest times. We have no reliable data as to the age and extent of the practice; we must be satisfied with the knowledge that a method of inoculating the virus into the skin or in the form of dry powder blown into the nostrils, has been known to exist before it reached Europe.¹³ In India a similar method seems to have been carried out on a systematic plan by special delegates of the Brahmin caste in conjunction with a religious cult of the smallpox deity.¹⁴

None of these primitive variolations served to acquaint [71] Western Europe with the practice. Only after it had reached a certain development in Constantinople could it be studied, reported and recommended. From this city Lady Mary Wortley Montagu, wife of the British Ambassador to the Porte, wrote to her friends at home about the method of inoculation as practised under her eyes and expressed her intention (to Sarah Chiswell, April 1, 1717, from Adrianople) of introducing it to England. She even caused the inoculation of her three-year old son Edward, by a Greek woman with Maitland's assistance,¹⁵ and influenced that of the three children of the Marquis de Châteauneuf, Secretary to the French Embassy at about the same time (1718). Her inspiration and these examples undoubtedly opened the doors for the in-

¹² Other reports from travellers about variolation: Bruce (1790), Levaillant (1790-1796), Michaux (ab. 1800) for Africa, Cook (ab. 1780) for Senegambia, Barbary, Bengal.

¹³ The "Tchan-teoo" or "sowing the smallpox" in d'Entrecolles, *Lettres édif. et cur. des missions* 1726, XX, 34 (from Pekin) and other reports in same letters.

¹⁴ Holwell, *op. cit.* Also J. Moore, *History of the Smallpox*, Lond., 1815, 26-34, with plate representing the religious rite, from a Hindu drawing in the library of Mrs. Bliss of Kensington.

¹⁵ Letter to Lord Montagu (of March 23, 1718) at Pera from Belgrad.

[71] troduction of the practice in England. There was already some medical agitation on the subject, before Lady Mary became interested, and it can safely be presumed that she was not ignorant of it. Dr. Timoni, a Greek physician of Constantinople educated at Oxford, published in 1713 an account of the method of variolation as observed and practised by him. In December of the same year he sent a personal communication on the subject to Dr. Woodward,¹⁶ who read it before the Royal Society. A little earlier a similar report reached the Swedes, sent to them from Bender in Bessarabia by their exiled king, Charles XII, with the recommendation to introduce the method.¹⁷

Other medical men in England at this time had some personal knowledge of the method which they had seen practised in Constantinople. We know of two, a Dr. Terry of Enfield, who later is consulted about it by Sir Hans Sloane, and a Scotch surgeon, Peter Kennedy,¹⁸ who describes the method in his book in 1715. A dissertation on inoculation appears in Venice by a Dr. Pylarini¹⁹ the next year. A friend and former consular colleague of the latter in Smyrna, Dr. Wm. Sherard, informs Sir Hans Sloane and, through him, the Royal Society, of this publication with details about the method and an account of Dr. Pylarini's experiences. Now the Royal Society becomes really interested and the pages of the Philosophical Transactions of the following years are filled with further accounts, which Douglass of Boston later (1730) characterizes sneeringly as "virtuoso amusements."

At the same time something was heard of the "Greek

¹⁶ John Woodward (1665-1728) excellent geologist, but poor physician. See Creighton's (*op. cit.*, p. 449) amusing account of his duel with Mead in Gresham College where he was professor of physic. Its cause, the smallpox controversy, involved also Friend and later Dover. In 1718 he published a tract "the State of Physick" in which he discussed the "new practice of purgeing" in smallpox.

¹⁷ This report was probably written by the king's physician, Skraggenstyerna.

¹⁸ Peter Kennedy: *Essay on external remedies* (Chap. 37), 1715.

¹⁹ Pylarini, *Nova et tuta, etc.*, 1715. Sloane in *Phil. Trans.*, XXIX, 1716.

method" in France. Boyer²⁰ of Montpellier, later Dean of [71] the Medical Faculty of Paris (1756), had travelled as a young man in the Orient and had there become acquainted with variolation. On his return to Montpellier he studied medicine and wrote his inaugural thesis (1717) on inoculation and the reasons why it might be imitated to great advantage in France. Actual inoculations very probably were practised in Paris at about this time by a Greek physician Carazza. Eller tells us of making his acquaintance there, and how he was taught the method and how he successfully inoculated a child. Although Eller does not mention the exact date, it is evident that it took place in or before 1720, because in that year he went with Lord Peterborough to England and returned from there to Germany in January 1721.²¹

At this moment, when the new method knocked at the doors of the universities, promising fresh hopes but also planting the first seeds of discord among the sister faculties, the 18th century is yet young. The glaring contrasts and contradictions are not as apparent as they will become later, the genius of Newton—he still presides over the Royal Society—is only beginning to assert itself. In medicine Sydenham's influence is paramount, while Boerhaave in Leyden and Morgagni in Padua are training men who are to found modern medical science. Hoffmann and Stahl supply the cravings for theoretical contemplation, while practice continues on old lines. Everywhere reform is in the air, the struggle against superstition and for tolerance has begun. The realization that

²⁰ J. B. N. Boyer, 1693-1768.

²¹ J. Th. Eller, *Observationes cognoscendis et curandis morbis praesertim acutis*, Regimont. & Lips, 1762, p. 150. (French transl. Par. 1774.) Eller was born in the Duchy of Anhalt in 1689, became M. D. in 1716 then travelled in Holland and practised in the mines of the Harz Mountains. From here he went to Paris and worked under Hecquet, Astruc, Helvetius and Winslow, giving much attention to surgery, at the Hôtel Dieu and the Salpêtrière. In London he frequented Cheselden, Mead, Sloane and Newton. He left London in January, 1721, became court physician in Anhalt, inoculated several persons, and in 1724 he was at the court of Berlin, teaching at the newly founded Medico-Surgical College. He and Stahl (Halle) are largely responsible for the sanitary reform in Prussia, which formed the basis for the present institutions.

[71] the riddles of life and its problems are not to be solved by pure metaphysical speculation begins to dawn upon the learned and experiment is more and more resorted to for the final criterion.

From the time of its introduction to the Occident in 1713 to the advent of vaccination in 1798 and its general acceptance in 1840, variolation does not follow a course of steady progress. As we shall see, it enjoys a few years of the success of novelty (until 1727), followed by twenty years (1746) of indifference, after which it slowly gives rise to a remarkable period of serious scientific investigation.

The honors of the first inoculation in the Occident (excepting that by Eller in Paris) will probably best be divided between London and Boston. Dr. Fitz, in an admirable account of the early inoculations in Boston, tends to the belief that Boylston, inspired by Cotton Mather, made his first attempt [72] without knowing of the inoculations performed in London.²² There is no direct evidence of his ignorance and he certainly had time to learn about the London inoculations in April and May, since he inoculated his son Thomas and the two slaves on June 26. Undoubtedly he had courage enough to proceed without any other assurance than that of his friends and the older reports at hand, but the situation was precarious and it looks as if the latest news may have been welcome and actually determined him.

The merits of Lady Montagu in inciting the early trials in London were undoubtedly great in that year of 1721, when the smallpox was raging on both sides of the Atlantic. A Portuguese physician in London, à Castro, had anonymously published a pamphlet on the subject in March and Dr. Walter Harris spoke recommendingly of inoculation before the College of Physicians on April 17. Lady Mary probably did not need these learned suggestions to remind her of her experience in the Orient and with the danger of smallpox at the door, she

²² Professor Kittredge (*op. cit.*) has recently given valuable additional information on the subject of early variolation in Boston. It leads to the conclusion that Cotton Mather's knowledge of it has not been fully recognized and especially that he was acquainted with variolation (among negroes) before he received the reports about it from Europe.

had Maitland inoculate, in April, her four-year old daughter, [72] the future Lady Bute. One of the three interested spectators from the College of Physicians, Dr. Keith, was sufficiently impressed by the harmlessness of the operation to have his own six-year old son inoculated on May 11. In this case, bleeding was resorted to as a preparatory measure and we see herein, as also in similar examples in Boston, the germ of that "preparation" which is to play such an important rôle later on. Lady Mary meanwhile does not stop with the inoculation of her own child; she takes up the personal propaganda begun in her letters from the Orient, she finds it now easy to induce many of her friends to follow her example, but her main efforts she exerts towards winning the court. In this task she is aided by her intimate relationship with the Princess of Wales, later Queen Caroline, whom Voltaire, because of her intelligent interest in arts and sciences, addresses as the "philosopher on the throne." George I is willing to permit the inoculation of his grandchildren but a preliminary experiment is deemed advisable. Here is the first beginning of scientific procedure. Six condemned criminals in Newgate prison are inoculated as test cases, the best medical men of London are watching the experiment, with Mead at their head. Nothing unusual happens; somewhat severe symptoms are observed only in one girl, whom Mead inoculated with dried virus in the nostrils (Chinese method), but she also recovers. One man in whom the inoculation did not "take," is found to have had smallpox before. A further test is made by Mead and Steigerthal, who send one of the inoculated patients to Hertford where a severe epidemic rages; no infection takes place. George I and his court feel reassured by the results of these experiments, and further good reports having reached the town from Halifax, in Yorkshire, where Nettleton had inoculated with satisfactory results since December, the operations on the Princesses Amelia and Caroline take place on April 19, 1722. The surgeon Amyand, attended by Sir Hans Sloane, Teissier and Maitland, performs the inoculation.²³ The immediate result of this evident approval of variolation

²³ A medal was struck to celebrate the event. *Av. George I, 1721, Rev. Inoculation instituted.* (Pfeiffer, 373a.)

[72] by the court was that the nobility hastened to follow the august example and so we find the gazettes reporting on these events, mentioning all the names of the ultra-fashionables. The next result was the formation of two opposing factions. Pamphlets were written, sermons preached for and against the new method, mostly by people who knew nothing or next to nothing about inoculation. This condition continues through the whole epoch of variolation and as a matter of fact long after its abandonment. In the vast literature thereby produced it is often exceedingly difficult to find one's way. Wagstaff, the medical satirist, Blackmore, inferior medical author and poet, Clinch, the surgeon, Massey, the apothecary of Christ Hospital, are the chief opponents; the learned Dr. Freind²⁴ wavers, but objects to the noise made about inoculation, Arbuthnot, friend of Pope and Swift and commentator of Boerhaave, Jurin, secretary of the Royal Society under Newton, Mead and Sloane were, however, more or less active in the recommendation of inoculation.

The arguments brought forth against variolation were, its risks to the individual, the uncertainty of its protective power and the danger of its spreading the disease. The last argument had received support when the news came of an accident that had happened in Maitland's experience at Hertford, where he had gone to inoculate in the autumn of 1721. A child ill with artificial smallpox had infected six servants of whom one had died. This demonstration of the contagiousness of inoculated smallpox offered the strongest point to the cause of the opponents. They, however, resorted oftenest to personal vituperation or bitter condemnation on religious and moral grounds. On the other hand the inoculators and their up-holders, although reiterating the most obvious advantages of inoculation, viz., freedom in the selection of appropriate subjects (children), favorable external circumstances (seasons), and careful preparation, resorted almost exclusively to statistical data in their support. Jurin,²⁵ who excelled in mathe-

²⁴ See reference to John Gaddesden in his "History" (1725): had he "lived in our day, he would, I don't question, have been at the head of the inoculators." (Creighton II, 478.)

²⁵ Jurin to Cotesworth 1723. James Jurin born 1684, secretary and later president of Royal Society, was one of the first physicians

matics, soon collected enough cases to figure out the ratios as: [72] One death only in 91 inoculated (two in 182), while the natural smallpox killed one in five or six. He refers to the "letter of Cotton Mather of the 10. March 1721" ²⁶ in which five to six deaths are reported among 300 inoculations, making a ratio of one in 60. He concludes from it that inoculators in New England were less careful. [73]

The technique meanwhile had seen considerable deviations from its primitive Greek prototype. In Constantinople, Maitland had already replaced the dirty needle of the woman operator by the lancet. Nettleton, who probably had the largest experience in these early years, thought it important to make rather deep incisions and to keep them open so that the wound would drain freely and allow the morbid humors to escape. The arms or thighs were the favorite regions chosen.²⁸ The virus was taken directly from a smallpox patient and transferred, or it was collected on threads and dried for later use.

It seems that the inoculations were not often performed by the physicians themselves; they usually had a surgeon do it and watched the case before and after. Thus a type of inoculation specialist was evolved and all sorts of people took it up as a lucrative profession.²⁹ Some of the failures may easily be attributed to crude methods. Maitland seems to have created the type of the itinerant inoculator, whom we can soon follow all over Europe. We have already encountered Maitland in Hertford; a few years afterwards he is on the continent inoculating Prince Frederick and others at Hanover. After this we

to Guy's Hospital. The advocacy of his "lixivium lithontripticum" brought him questionable fame.

²⁶ A. L. (contemporary copy) in Sloane MSS. 3324, fol. 260 (see Kittredge, *op. cit.*, p. 477). The letter is also quoted by Douglass in his "dissertation" of 1730.

²⁷ The figures of Cotton Mather are quoted by the anti-inoculists again and again with considerable success all over Europe.

²⁸ In the Greek practice the forehead, shoulders, hands and other parts of the body were chosen, the choice being determined on religious grounds and it varied with individual inoculators.

²⁹ We know of a blacksmith who thus changed his occupation, and a man-servant who gave notice to his employer because he could earn more as an inoculator. (Wāts, Watson.)

[73] find him in Scotland ³⁰ where he has ill-luck, losing one in ten. This experience, the Hertford case, and the deaths of several prominent persons, duly registered in the gazettes, added powerfully to the arguments of the opponents. The subject was brought up in Parliament and inoculation declared dangerous. This was in 1728. Up to that year Jurin ³¹ could collect in his report 897 known inoculations with 17 deaths, not all directly attributable to the operation. He considered the practice now "exploded," while the otherwise sceptical Douglass ³² admits that the opponents are now prepared to acknowledge that "inoculation, generally speaking, is a more easy way of undergoing smallpox."

The Continent, meanwhile, did hardly more than act the part of the spectator. LeDuc of Constantinople writes the first inaugural thesis on inoculation at Leyden; it is approved on July 28, 1721, and published together with the dissertations of à Castro and Walter Harris of London in 1722. Boerhaave maintained an expectant attitude. We have no reports of his having tried the method himself or persuaded others to do so. Theoretically he surely approved, for we find him saying at the end of his Aphorism 1403 (Edit., Leyd., 1727). *Prophylaxis insitiva videtur satis certa tutaque.* Of his pupils Van Swieten continues in this reserved attitude, while de Haën becomes one of its most persistent opponents and Tronchin one of the most famous inoculators in Europe.

In Germany Eller, whom we have met already in Paris, has returned to his home in Anhalt. As physician to the local court he performs two inoculations, but, soon called to the Prussian court, he is not allowed to see smallpox cases and has to desist. In Breslau reports are received of inoculations performed by one Reimarus in Hungary.³³ In the two universities, Altdorf and Erfurt, which have long ceased to exist, doctor dissertations are published on inoculation by Mülich

³⁰ Alex. Monro I, 1697-1767.

³¹ See also Scheuchzer (son of the Zurich naturalist) on success in Great Britain, 1729. Another late endorser of the method was Lobb in 1831. (His treatise on smallpox received the praise of Boerhaave.)

³² Douglass, 1730, *op. cit.*

³³ Breslauer Versuche, XVII, 253.

and Cramer,³⁴ but they report no new trials. In Hanover, [73] however, the inoculation of Prince Frederick acted as a stimulant. J. E. Wreden publishes a treatise on it and his son John, later body surgeon to the Prince of Wales, soon begins to inoculate.³⁵ Outside of the Electorate of Hanover, naturally influenced by England, Germany contributes very little to the history of inoculation. Of Austria, Italy and Switzerland I shall speak later. In Sweden we have one publication in 1737 by Spoering, but also no actual inoculation.

The history of variolation in France offers much of interest and forms a valuable contribution to the annals of culture in general. At the time when variolation first appeared in England, medical science and practice in France had made little progress since the days of Ambroise Paré and Guy Patin. Montpellier showed more signs of progressive activity and in later years especially, the children of this Alma Mater were prominent in the ensuing struggle. While in England inoculation occupied minds rather intensely for eight years, only in the one year of 1723 is this subject at all considered in France, particularly in Paris, and then only academically. Louis XV was then thirteen years old and the Duke of Orleans was nearing the end of his regency and his life. Dr. de la Coste, an enthusiast for inoculation, who had followed its introduction to England, writes about it to Dodart,³⁶ formerly physician to Louis XIV. He tells him all he knows about the subject and especially that the English court is in favor of it. At a solemn meeting at the Sorbonne he explains to the learned dean and nine doctors the evident advantages of inoculation. After a careful analysis of the moral and religious factors involved, it was decided that experiments might be made without interfering seriously with Divine providence. This meeting had the effect of winning over the Regent, who also probably was influenced favorably by Helvetius³⁷ who was close to him at the time. It therefore looked for a while as if experiments might begin. Then

³⁴ 1725 and 1726.

³⁵ Report in 1739, London.

³⁶ Cl. J. B. Dodart, 1664-1730.

³⁷ J. Cl. Adr. Helvetius, 1685-1755.

[73] appeared an anonymous pamphlet entitled: *Raisons de doute contre l'inoculation*, in which strong language was used against *la méthode anglaise* and its promoters. It [74] was soon learned that the author was old Hecquet,³⁸ dean of the *Faculté de médecine*, more theologian than physician and a stubborn opponent of all innovations. His words carried much weight and when the Regent died on December 3, the chance of inoculation grew very faint and was entirely extinguished at a meeting in the *École de Médecine* on December 30³⁹ where the *quæstio medica*, worded ominously "Is it a crime to inoculate?" was discussed under the presidency of Claude de la Vigne,⁴⁰ the new king's new physician. An interesting contrast: the Sorbonne for, the *École de Médecine* against the new method! As a child Louis XV comes to power; he was of course not to blame in that, for 30 years after his advent, inoculation was hardly mentioned in France, but curiously enough, as a man, after 50 years of a disastrous reign, he falls victim to the very disease the method was intended to prevent. Voltaire, in his apartment quite close to the *École de Médecine*, at this moment is making a very personal and most unpleasant acquaintance with smallpox, nursed by his devoted friend Adrienne Lecouvreur. Two or three years hence he is to begin his eloquent propaganda for inoculation in one of his letters from that England which is to influence so strongly his whole point of view.

During the 20 years following the practical abandonment of inoculation in England, and while next to nothing was done in Europe, events occur in America which later are to help considerably towards a revival of the practice. An epidemic of smallpox in Charleston in 1738 gives the incentive. A surgeon, Mowbray, and a Scotch physician, Kilpatrick (later as Kirkpatrick one of the foremost inoculators in England), inoculate a very considerable number of persons in that year.⁴¹ Mowbray evidently started the inoculations

³⁸ Phil. Hecquet, 1661-1731.

³⁹ Duvrac's account, 1755.

⁴⁰ Cl. de la Vigne de Frécheville, 1695-1758.

⁴¹ Kilpatrick, *op. cit.*, p. 44. On May 21, 1738, the first three persons were inoculated in Charleston, the two daughters of a Mrs. Sarah Blakeway and a Miss Baker.

and seems to have done the greatest number. Kilpatrick's [74] account, which was published first in Charleston and then in London in 1743, relates, with great frankness, the successes and failures (about 800 inoculations with eight deaths).⁴² They met with distinct opposition, especially on the part of other practitioners.⁴³ Kilpatrick, in theory, favors careful preparation of the patient before the operation. His guiding principle is the cooling regimen of Sydenham with a "few remedies perhaps" so that the "Solids and Fluids may be reduced from a greater, to less Inflammability." His conception, as these quotations show, is that of his time but he admits, "without prejudice, that preparation was too often neglected with us." We also learn from him, and this is an important innovation, that Mowbray very often inoculated with the virus taken from the pustules of a previous inoculation and that he repeated the process up to six times,⁴⁴ without perceiving any reduction of virulence. It would be interesting to enter more fully into the excellent observations of this essay. They are distinctly in advance of the time and I believe mark a more valuable advance in the history of inoculation in America than that presented in a pamphlet of Dr. Adam Thomson, published eight years later and of which Dr. Henry Lee Smith⁴⁵ has given a full account. From this "discourse" of Thomson's it appears that he had begun to inoculate in Philadelphia at about the same time when Mowbray and Kilpatrick started their experiments in Charleston. The crux of his method is specific preparation, applying Boerhaave's suggestion that mercury and antimony may act as preventives against smallpox. He lays greater stress on these medicines than does Kilpatrick, otherwise there is no difference between the two methods. There is no doubt that Thomson succeeded in impressing his patients and also some doctors with his method of preparation. Dr. Gale of Connecticut seems to have been his most enthusiastic follower. At least I find him writing to Huxham⁴⁶ about it: Boerhaave's

⁴² Kilpatrick, *op. cit.*, p. 34.

⁴³ Kilpatrick, *op. cit.*, p. 44, controversy with Dr. Thomas Dale.

⁴⁴ Kilpatrick, *op. cit.*, pp. 49 and 50.

⁴⁵ Johns Hopkins Hosp. Bull., 1909, XX, 49.

⁴⁶ John Andrew, 1765, *op. cit.*, pp. 9 and 44.

[74] "intimation was improved, and mercury introduced into practice, by physicians in the English American Colonies, about 1745. Several American physicians claim the second glory of Boerhaave; perhaps Dr. Thomas (*sic.*) of Virginia, and Dr. Murison of Long Island." Ruston "a little later in speaking of this method ascribes it, as does Gale, to Murison and to Dr. Thomson of Virginia. Ruston who is in favor of a mild preparation, shies at this particular one for the secret of which, he says, "considerable premiums were offered." Ten to twenty grains of calomel every other night counteracted by a drastic purgative for two weeks seem to him rather violent as a preparation for more trouble!

We are now nearing the middle of the 18th century. The failures of the introductory period in England were almost forgotten and Europe in general was becoming more and more receptive to such an innovation and, with the increasing restlessness of the age, receptiveness developed into eagerness. In England Kilpatrick's essay (1743) on the experience in South Carolina was very largely responsible for a revival. He had arrived himself and at once set to work as a specialist inoculator. Among those who followed his example are Ranby, Middleton, Hawkins, Frewen, Burges, Archer, etc. The alleged necessity of an elaborate course of preparation on hygienic and medicinal lines, of a surgical operation requiring often a prolonged after-treatment, held out golden promises to physician, surgeon and apothecary. Mercenary calculation therefore entered very largely into the advocacy of "preparation" and deep incisions. It is well to bear this in mind. Some of the more earnest practitioners object to these complications but, in spite of them, this cumbersome procedure maintains its vogue during the following 20 years. The fact that it is very costly rather increases the demand for it among the wealthy and thus it gains influential protectors. This leads to provision for the poor and here the foundation, under the patronage of the Duke of Marlborough, [75] of the Middlesex County Hospital for smallpox, and soon afterwards that of others in London,⁴⁷ marks an epoch. There

⁴⁷ Thomas Ruston, *op. cit.*, p. 2.

⁴⁸ This hospital changed its location several times shortly after its opening in Windmill Street, to Mortimer Street and finally to

was little effort made, at least at first, to utilize these institutions for a scientific study and an improvement of variolation. [75]

As each patient, because of the preparation before inoculation, had to stay a very long time, at least while a preparatory period was thought to be necessary, the benefit which the poor derived from these hospitals was very small, because of the few that could be admitted.

The practice of variolation, thus taken up in all earnest by energetic medical men, prevailed in spite of the opposition which continued unabated. The cause found a very valuable champion in Isaac Maddox, Bishop of Worcester, who in his sermons intelligently and forcefully recommended inoculation. Another churchman, de la Faye, on the other hand, used the pulpit for the fiercest denunciation of inoculation and inoculators. In medical circles all the questions involving smallpox and variolation were ventilated. The war of pamphlets is opened by a letter of one Dod Pierce to Pierce Dod, physician of St. Bartholomew and author of "Several cases in physic."⁴⁹

In 1747 Mead's *de variolis* (with the translation of Rhazes' commentary) appears. He devotes a brief chapter (V) to inoculation. He is decidedly in favor of it and does not

Lower Street, Islington. The other hospital soon after opened at Bethnal Green (44 beds). After 1750 15 patients could be received, prepared and inoculated at the Inoculation Hospital in Old Street, St. Luke's, whence they were taken for after-treatment to the hospital at Fray Lane. In 1752 the governors of Charity opened another large smallpox hospital at Coldbath Fields (130 beds) also for preparation previous to inoculation.

⁴⁹ I do not find this delightful biting satire mentioned in any history of inoculation and it well deserves notice as it gives an invaluable picture of the manner of thought among certain physicians of the day. The author, it may well be Kirkpatrick, pretends that he is trying to expose "the low Absurdity, or Malice, of a late spurious Pamphlet, falsely ascribed" to Dr. Dod, and aims particularly at his principal case in physic: "giving an account of a person who was inoculated for the smallpox, and had the smallpox on the inoculation, and yet had it again." With banter and derision, jeering and sarcasm, he parodies Dod's bungling, awkward language, denounces his absurd reasonings and faulty observations. (In the Surgeon-General's Catalogue the author is given as W. Barrowby.)

[75] know of relapses after it. According to him the great advantage of the inoculated disease over the natural one is the opportunity afforded of selecting appropriate subjects and preparing them "by drawing away, where necessary, some blood, and gently purging the humors," in order to "obviate the violence of the approaching fever." He cannot imagine much benefit from the discharge of the wound of inoculation and in general finds the artificial disease so mild that it hardly calls for help from any physician. This common-sense point of view was not shared by the majority of inoculators, in whose interest it was to emphasize the importance and gravity of the operation. But Mead's great influence and authority helps to smooth the path for the method. And indeed, all through the following years and considerably into the 19th century, we see variolation in England in continual progress. I need not enter into the details of its historic evolution here, since this has been admirably done by Creighton. It may be sufficient to point out that in the first 20 years of the revival, during which the method was exploited by more or less unscrupulous practitioners as a lucrative occupation, we do not find many evidences of a scientific improvement. In Kirkpatrick, Mead and Frewen we can already observe attempts at simplification and a desire for a better understanding of the fundamental questions involved. But it is only after 1764 with the advent of Gatti, the Suttons, Dimsdale, Watson, Mudge, Maty, Lettsom and others that a more scientific, systematic spirit is infused into the growing movement.

The tendency now becomes manifest to "prepare" chiefly by hygienic and dietetic means and to abandon frequent bleedings and violent purgation. The Suttons⁵⁰ have certainly a great share in the vulgarization of this practice. The mystery with which they surrounded their method and their

⁵⁰ Of Robert Sutton we hear already in 1753 as an inoculator in Suffolk, where he experiments on himself and soon starts the business with three sons and a son-in-law, Dr. Hewit. Ten years afterwards his eldest son leaves him and begins on his own account at Ingatestone near Chelmsford (Essex), where he opens a hospital for inoculation and starts a flourishing enterprise with ramifications all over Great Britain and the Continent; his partner and assistants were Peale, Worlok, Sutherland and others.

successful avoidance of accidents were powerful factors in [75] their favor. Their hygiene consisted mainly in a continuous open-air life before inoculation and during convalescence, to which were joined cold water applications. The secret remedies which they administered played probably an inferior rôle in the régime, though in popular belief they were assigned an important position. Their analysis (Ruston) showed them to contain the ingredients of Boerhaave's antidote (calomel and aethiops mineralis) and of the popular preventive pills of Schulz and others (cocolcynth, aloes, cloves, etc.).

Of greater importance in Daniel Sutton's régime were probably the attempts at attenuation of the virus itself and, in this regard, he probably learned from others, from Kirkpatrick and especially from Gatti, although it cannot be doubted that he himself was a capable observer and experimenter.⁵¹ Attenuation of the virus was to be obtained in various ways: first by passing it through several human subjects (Kirkpatrick's arm-to-arm method),⁵² by inoculating very small quantities of the virus and particularly by choosing it at the proper moment of development (the crude, unripe stage). We find all these points already suggested in Kirkpatrick's Charleston essay and, in passing, we may mention that Beddoes had tried to attenuate the virus by dilution with water, Woensel by mixing calomel with it, Kirkpatrick proposing camphor and other "scents."⁵³

These efforts were all in the right direction, only it appeared, particularly after Dimsdale⁵⁴ legitimized Sutton's [76] method, that the attenuation was often carried so far that the result of the inoculation was sufficient to confer the desired immunity. Hence examples of relapses were cited and Bromfeild⁵⁵ had a right to fear that inoculation might become disgraced.

⁵¹ George Baker in 1766 tells us of Sutton's attempts at inoculating measles with the conjunctival fluid of patients.

⁵² Thomas Frewen and others had already inoculated by this method in 1749 and abandoned Nettleton's deep incisions. Sutton seems to have avoided the virus from smallpox cases altogether.

⁵³ The admixture of musk to the virus practised by the Chinese may have had a similar motive.

⁵⁴ Thomas Dimsdale, 1712-1800.

⁵⁵ William Bromfeild, 1712-1792.

[76] Sutton, Dimsdale and the others who adopted the "new method" did away effectually with the deep incisions, inaugurated by Nettleton and defended with so much tenacity. Slight punctures or scratches were now found to be amply sufficient and the disagreeable after treatment of the wounds was thus prevented. Tronchin introduced the virus into an artificial blister, a method followed extensively on the Continent and also intended to avoid the prolonged suppuration of the wound. This found little favor in England.

Thus the operation had reached a degree of simplicity, and lessened discomfort and danger, not thought possible before. Only the question of the protective value remained open. We remember that vaccination passed through similar phases and that relatively very late the necessity of re-vaccination became apparent. The test of repeated inoculations was resorted to quite frequently; we find reports of it all through the literature of those days. But experiments were also made to determine which part of the new régime and what kind of virus guaranteed the success of the operation. Watson,⁵⁶ who was physician at the Foundling Hospital where all children were inoculated, made some interesting experiments in 1767. Gatti was at that time in London and saw Watson often, which makes it very probable that he played some active part in them. Watson chose three parallel series of cases, 31 were inoculated with the virus from a smallpox case in the ichorous or watery state, 23 from another inoculated patient, but in the purulent state, and 20 others also from artificial smallpox with virus "in perfectly concocted state." This latter series was not "prepared" before inoculation, while the others went through the customary dietetic preparation (10 of the first series with calomel before and after inoculation). All of the patients were "out in the fields during the whole process." Watson gives a careful analysis of the results observed, some even in tabulated form, from which, as he puts it, every person is at liberty to make such deductions as he may think they will admit of. His personal conclusion is that the choice of the virus is not very material, that the ichor gives slightly better results, that the mercury has no specific effect and only

⁵⁶ William Watson, 1715-1787.

acts favorably as a mild purgative. A well regulated vegetable [76] diet before and during the whole process, the avoidance of heated rooms and heating liquors, he believes to be advantageous but not essential.

Re-inoculation experiments were undertaken by John Mudge⁵⁷ of Plymouth. Forty inoculations were made and seemed to demonstrate that "crude" matter taken from inoculation vesicles five days old does not convey immunity against a re-infection with natural or inoculated virus.

It is not evident that the results of these and other experiments exerted any revolutionizing influence on the method used earlier, but they must have helped towards perfecting it. The operation as then practised seems to have given satisfaction, for inoculations certainly became very popular in England, so much so that vaccination, in spite of the advantages which to us seem very clear, had first to subdue variolation before it could make any appreciable headway. It took exactly 44 years after Jenner's first vaccination, when, by act of Parliament, variolation was declared a felony.

Throughout this stage of evolution the Continent of Europe, in matters of variolation, is influenced by England. We see physicians arrive in London from various parts of Europe to study the method and on the other hand professional English inoculators travel all over the Continent to perform the operation, helping thereby its introduction.⁵⁸ Nowhere, however, did the practice reach the extent it had in England, although there is more noise about it and publications abound. This is a curious and notable fact, particularly when one considers that vaccination later was taken up in some continental countries more immediately and readily than in England. The first insistent plea for the introduction of variolation to the Continent was made by Voltaire from England where during his three years sojourn (after 1726) he had heard it discussed

⁵⁷ For details the original ought to be consulted, also Creighton *op. cit.*, pp. 501 and 502.

⁵⁸ See Ebstein (*op. cit.*) about inoculations by George Motherby in Koenigsberg; Seitz about Baylies in Germany in *Arch. d. Gesch. d. Med.* II, 410; Chais (*op. cit.*) about Sutherland in Holland; Gardane (*op. cit.*) about Worlok and Seeby in France; Power (*op. cit.*) also in France.

[76] and had seen it practised in that country. That friend of John Locke's, Lord Peterborough, who, as we have seen, had brought Eller from Paris to London, took him also to his house. Voltaire made himself acquainted with everybody and everything with that eagerness so characteristic of him. Inoculation was on the wane just then, but its fundamental importance did not escape his keen mind. One of the many letters addressed to Theriot from England ⁵⁹ is devoted to the subject of "l'insertion de la petite vérole." It is a most eloquent appeal. Motives common to all people, maternal tenderness and selfish interest,⁶⁰ he says, introduced inoculation to the Circassians. Then, by experience and observation of the disease and its peculiarities, this primitive people gradually evolves the idea of protective inoculation. How much more [77] can an advanced nation profit from this by perfecting the method! And Voltaire did not, after the manner of some *philosophes*, stop with this one dramatic appeal. We find that through his life he continues to exert his influence in favor of the method. Thus it was he who persuaded Catherine the Great, of Russia, to undergo the operation. Dimsdale was called (1768) and also inoculated the Grand Duke Paul and many nobles and others in St. Petersburg and Moscow. Returning he left in his wake an inoculation hospital here and indirectly one other in Irkutsk, Siberia! Indeed an evidence of Voltaire's far-reaching influence!

France was, however, not yet ready for inoculation. Only 20 years later did it receive a general consideration. The reason for this is not very easy to understand. De Mariveaux

⁵⁹ "Lettres philosophiques," at first called "Lettres sur les Anglais." Letter IX written in 1727 and also published in "Dictionnaire Philosophique," 1764.

⁶⁰ The Circassian and Georgian beauties were much in demand for the Turkish harems. Voltaire found the story of the Circassian origin of inoculation in de la Motraye's *Voyages*, etc., *La Haye*, 1727. Later travellers in the Caucasus found nowhere signs of inoculation being practised there. Creighton waxes indignant about this "myth constructed in cold blood." He thinks it is given "as a mere assertion in the manner of a *philosophe*" and therefore needs no refutation, whereupon he proceeds to give a long one. Evidently he is not Voltaire's friend. (*Creighton, op. cit.*, II, 473, note.)

in a reply to that letter of Voltaire's explained it thus: *si [77] nous n'inoculons pas en France comme en Angleterre, c'est parce que les Anglais se décident par le calcul, et nous par le sentiment.* Whatever the reasons may have been, the fact remains and we know only of isolated trials, principally in Paris. We must note here one serious effort which seems to have escaped most historians. Tenon, the excellent surgeon of the Salpêtrière, on his return from the campaign in Flanders (1745), quietly establishes an inoculation service in special premises annexed to the hospital. His interest in inoculation becomes evident only 10 years later when he inoculates the Comte de Châtelux, who in turn becomes an ardent champion of the cause. While Frenchmen on the whole were indifferent to the English example, the little republic of Geneva⁶¹ had among its citizens men who evinced a distinct interest for everything English. Thus it may be explained how very early and determined efforts to introduce inoculation were made there. Already in 1748, Tronchin,⁶² a Genevese settled for some years in Amsterdam, the favorite pupil of the old Boerhaave, had inoculated first his own son and then continued the practice among his patients. He introduced it also to Geneva where, on a visit in the summer of 1749, he inoculated a nephew, the son of the philosopher and magistrate Colandrini. Then the surgeon Guyot began to inoculate in September, 1750, and was soon followed by two physicians, Cramer and Joly. Trembley, the naturalist, another Genevese, had seen inoculations done in England and on the occasion of a visit to his home he suggested experiments in the hospital which were undertaken with encouraging results. In 1752 Guyot could report to Paris on his first 33 cases and others give accounts of even more, among them Buttini, who publishes an excellent essay. The practice is in full swing when Tronchin returns to Geneva (1754) and strangers flock into the town to be inoculated. In neighboring Lausanne

⁶¹ L. Gautier, *La Médecine à Genève*, 1906, p. 391. Gautier gives in this interesting medical history a full account of the progress of inoculation in Geneva.

⁶² Theodore Tronchin, 1709-1781; see his biography by H. Tronchin, *Par.* 1906.

[77] Tissot,⁶³ who is already enjoying considerable fame as a practitioner, has taken up inoculation and publishes, in 1754, a treatise which was to be one of the most read and quoted in all Europe. Tissot's warm friend in Berne, the great Haller, has his own daughter inoculated and becomes active in its recommendation. J. Bernoulli does the same in Bâle and gives an address on the subject at the University. Mieg in the same town, S. Schinz and I. K. Rahn in Zurich, report on their results, but nowhere in this country we now call Switzerland does inoculation flourish as in Geneva, and it is here that it is carried to its logical consequences on a smaller scale but to the same effect as in England.

Two other countries, parts of what is now Germany and Sweden, also obtained their inspirations in the matter of variolation from England. Hanover, belonging to the English Crown, saw the first inoculations, as already told. Haller was in Göttingen from 1736 to 1753. There had been a little stir about inoculation in Hanover nearly 12 years before he arrived, when Maitland came to operate on Prince Frederick and Wreden had published his *Vernünftige Gedanken*. But those events were forgotten and Haller had more pressing things to attend to during his stay. That he took an active interest in the subject becomes evident a few years after his return to Berne in 1753. Another great man, Haller's friend Werlhoff,⁶⁴ at Hanover, was present at the inoculation of three other English princes in 1754, and from then on continued to inoculate together with Berger and others. Zimmermann,⁶⁵ who in 1768 replaced Werlhoff on the recommendation of Tissot and Haller, kept up an interest in inoculation. Murray,⁶⁶ in touch with England (Pringle) and Sweden (Schulz), writes excellent pleas. At Göttingen several inaugural dissertations were devoted to the subject (Grimmann, Houth and others under Schröder) after Roed-

⁶³ S. A. A. D. Tissot, 1728-1797, one of the most famous practitioners and prolific writers of the 18th century.

⁶⁴ P. G. Werlhoff, 1699-1767.

⁶⁵ J. G. Zimmermann, 1728-1795.

⁶⁶ J. A. M. Murray, 1740-1797.

erer,⁶⁷ Haller's successor, had shown the way. Wrisberg,⁶⁸ the [77] eminent anatomist, devised a special instrument, by which the depth of the incision could be regulated and we see later his great pupil, Soemmerring, as one of the earliest and most earnest supporters of vaccination. I have already referred to the English itinerant inoculators. At all the many little courts of Germany we see them appearing. Baylies⁶⁹ seems to have been the most active. His advent marks the introduction of the Suttonian method in Germany (announced by Wichmann in Hanover). Between 1767 and 1775 we can follow his tracks everywhere. Frederick the Great who, already in 1755, had expressed his astonishment that so little was done in Prussia for a promising method, calls Baylies to Berlin in 1775. He is to teach 14 physicians from the provinces his method in the hospital. We have notes on this course made by one of the physicians and from them it does not appear that the teacher had anything new to teach. Baylies had a dispute with Muzel, who, with the elder Meckel,⁷⁰ [78] had inoculated some persons several years before with very poor results, and this was probably the cause of his rather sudden departure. Other eminent men, Pastor Süssmilch,⁷¹ the founder of medical statistics, and Möhsen in Berlin, Ludwig in Leipzig,⁷² Tralles⁷³ in Breslau, Hensler,⁷⁴ the medical historian, and Juncker⁷⁵ in a special *Archiv*, plead the cause of inoculation, but these are all isolated instances without any marked practical results, reflecting the political chaos which was only very gradually focussing itself into a national unit. Only during the last decade of the century do inoculations become more numerous (Juncker) but these are soon given up in favor of vaccination.

⁶⁷ J. G. Roederer, 1726-1763.

⁶⁸ H. A. Wrisberg, 1739-1808.

⁶⁹ Will. Baylies of Bath, 1724-1789.

⁷⁰ J. F. Meckel, 1714-1774.

⁷¹ J. P. Süssmilch, 1707-1767.

⁷² Chr. G. Ludwig, 1709-1773. Among his many writings is one of peculiar interest in regard to the study of medicine, *De medicina studio non praecipitando*, 1772.

⁷³ B. L. Tralles, 1708-1797.

⁷⁴ P. G. Hensler, 1733-1805.

⁷⁵ J. C. W. Juncker, 1761-1800.

[78] In Sweden and Denmark also we see influences carried directly from England and Hanover. Of the progress in Sweden, Murray gives an excellent account and from Denmark Callisen⁷⁶ is able to report numerous inoculations. In both countries it is introduced at about the same time (1754 to 1756); in Sweden by a personal plea of the King on the advice of the medical college and the support of eminent men, among whom must be named Rosén, Bergius and Schulz,⁷⁷ the latter publishing one of the best treatises on variolation. By the initiative of these men Sweden was receiving very early the benefits of an excellent medical and sanitary organization and inoculation benefits by it. Already in 1757 we see inoculation hospitals (Gotenborg) founded and we learn from a letter of Baron Scheffer to la Condamine that systematic inoculations in the public schools of Stockholm are undertaken. In Copenhagen also an inoculation hospital is founded, after Baroness Bernsdorff, probably on the suggestion of Berger of Hanover, her physician, had submitted her children to the operation.

Tronchin's first inoculation did not immediately create a following in Holland. Only six years afterwards, in the year (1754), when he was leaving the country, we hear of the first inoculation performed by a Dutchman,⁷⁸ the excellent anatomist, Thomas Schwencke, at The Hague. In the same town inoculation finds an ardent defender in Pastor Chais and one of its most formidable opponents, Anton de Haën, who, however, is just leaving The Hague to go to Vienna. Thanks to the efforts of influential scientific men like Hovius and Camper⁷⁹ in Amsterdam, the interest in variolation is preserved and even carried to the Dutch Indies.⁸⁰

The greatness of Dutch medicine slowly vanishes after the death of Boerhaave. Van Swieten⁸¹ rapidly transplants the

⁷⁶ H. Callisen, 1740-1824.

⁷⁷ Nils Rosén (von Rosenstein), 1706-1773. P. J. Bergius, 1730-1790. Dav. Schulz (von Schulzenheim), 1732-1823.

⁷⁸ Van Leersum's account of inoculation in Holland in Janus, 1910, XV, 363.

⁷⁹ Jacob Hovius, 1710-1786; Petrus Camper, 1722-1789.

⁸⁰ van Hogendorp, v. d. Steeg, van Nielen (Batavia), *op. cit.*

⁸¹ Gerard van Swieten, 1700-1772.

spirit of the Leyden school to Vienna. To count Van Swieten [78] as one of the opponents to inoculation as is often done is not correct. We find him writing on July 23, 1755, to Dr. van Leempoel ⁸² from Vienna: "I am in favor of inoculation—and endeavor to introduce it here," and again in February, 1757, to de la Condamine that he is waiting for spring to begin experiments with it. It is not certain that these trials were then made, but we do know that later on experiments were certainly made with his consent and interested attention. The truth of the matter probably is that he kept above all parties. De Haën ⁸³ on the contrary, soon after his arrival in Vienna, proclaimed his sweeping condemnation of inoculation. In 1759, in his "Questiones," he asks: "Is inoculation permissible before God? Will inoculated smallpox spare more people's lives than the natural disease? Is it really true that almost everyone must get the smallpox? Is it not doubtful whether inoculation, after conveying the disease or not, protects against a new attack?" All these questions de Haën answered emphatically in the negative, but with little solid substantiation. His ruthless attack on the promoters of variolation caused a literary stir. Tralles in Breslau, Tissot in Lausanne and de la Condamine in Paris answered by letters which really were treatises. De Haën thereupon pronounced a summary "refutation" of inoculation. His character is extremely difficult to understand, but as a teacher of great merit he undoubtedly helped Van Swieten in the reorganization of the medical school, thereby establishing its fame. Though ultraconservative, still interested in processes against witchcraft, which explains his interest in the moral side of inoculation, he was one of the first to utilize the thermometer clinically, while percussion, or Haller's teaching, did not interest him. His bark, however, must have been worse than his bite for he does not seem to stem the incoming tide of inoculation in Vienna: The Empress Maria Theresa, 50 years old, having recovered from smallpox, in 1767, on the recommendation of Pringle, calls Jan Ingen-Housz, a Dutch pupil of Dimsdale's to Vienna for the inoculation of two archdukes and one

⁸² Janus, 1910, XV, 368 (van Leersum).

⁸³ Anton de Haën, 1704-1776.

[78] archduchess. The satisfactory result of the operation, after an extensive series of 200 test cases, opens the doors wide to the practice, which, particularly at the hands of Stoerck⁸⁴ and Locher, receives a thorough application and investigation. We have an excellent account of this period of inoculation in Vienna by Rechberger.

It remains now to review the subsequent fate of variolation in Paris, and in France and those countries more directly inspired from there. Paris was then, even more than it is now, the center of all activities in France and therefore it must appear strange that the most important local developments in regard to inoculation issued from two strangers, Tronchin and [79] Gatti. When Gatti⁸⁵ appeared in Paris from his home in Pisa in 1760 he found, as he expressed it, "more brochures for and against inoculation than inoculations." This must have been very near the truth all through the whole period of variolation in France, for nowhere do we find anything approaching the number of inoculations reported in England, while we have to make our way through innumerable books, letters, pamphlets, fugitive leaves, etc., in order to get at the actual facts. Plentiful ideas are exposed with characteristic vivacity and sprightliness but reports of actual experiments are meager. When they do occur they almost always evince clear and penetrating observations. The war of pamphlets began in 1754, when de la Condamine⁸⁶ returned from a voyage of exploration in South America, whence he brought back the exact measurements of an equatorial degree, cinchona bark, rubber and, what interests us most, a deep conviction of the value of inoculation. A Carmelite missionary in Para had seen something in a European gazette about inoculation and, smallpox being in evidence, he at once inoculated his flock with excellent results. De la Condamine had seen him and his experiments and became convinced. He had no medical training, his leaning was towards mathematics and he had entered

⁸⁴ Anton Frhr. von Stoerck, 1731-1803.

⁸⁵ Angelo Gatti of Mugello (Tuscany) was professor of medicine in Pisa.

⁸⁶ De la Condamine, 1701-1774. He had already, once before, in 1732, attempted to interest the Academy in inoculation but failed.

the Academy of Sciences, as he puts it, by the door of chemistry, the only one open. On April 24, 1754, a memorable day in the French annals of variolation, he addresses, for the first time, the Academy in favor of inoculation. His plea is based almost entirely on the English experiences as given in Kirkpatrick's "analysis" and some later publications including the reports from Geneva. As an embellishment are used the picturesque details of the "Greek method." It is one of those speeches the like of which we have often had occasion to hear in our own fight against the "white plague"; the danger is graphically described, the simplicity of the preventive means outlined, and the results to be achieved are mathematically fixed. "If inoculation had been introduced into France in 1723," concludes de la Condamine, "we would now have saved the lives of about one million people without counting their offspring." The effect of this address was that it stirred up great interest in inoculation. When one now reads the literature on inoculation which followed de la Condamine's *mémoire*, one gets the impression that, almost up to the advent of Dr. Guillotin's little instrument, nothing interested the French so much as how to save lives either with or without inoculation. That is probably what de Mariveaux meant by French *sentiment* as against English *calcul*!

Actual experiments, however, were very scarce. People in general, even those who took de la Condamine's views of the matter, seemed deadly afraid of the operation. We hear of the inoculation of some children on the advice of Turgot, a young lawyer and later a powerful minister. The Marquis de Châtelux was the first adult to go through the still dreaded test.⁸⁷ An example from royalty was much needed. In almost every European court variolation had entered comparatively easily, probably because a preventive was most anxiously desired in those palaces crowded by a suite often numbering into the thousands and thus offering particular dangers. The

⁸⁷ Buffon's words, when addressing de Châtelux at his reception to the French Academy in 1775, are: "Alone, without advice, in the flower of your youth, but decided by a maturity of reason, you went through the test then still dreaded."

[79] Duke of Orleans, grandson of the Regent, who, by his death in 1723, had disappointed the early hopes of inoculators, was now determined to make the experiment in spite of small encouragement from Louis XV. A friend of Tronchin's, de Jancourt, probably persuaded him, and Sézac,⁸⁸ who only later became an opponent, approved of it. Tronchin arrives very quietly and the operation is performed towards the end of March on the two children, the Duke de Chartres and Mlle. de Montpensier, with the assistance of Hosty and Kirkpatrick. Everything goes well and Tronchin is the hero of the day. The psychology of this moment and the individuality of the principal actors are most interestingly analyzed in the biography of Tronchin⁸⁹ by one of his descendants, reviewed for American readers by Dr. F. C. Shattuck. Tronchin's stay in Paris was short, he departed in June, but it seems that during that time he performed a number of inoculations among the nobility. I am inclined to think that the number was very small and when the *Duc de Luynes* in his memoirs (March 28, 1756) says: "Tronchin pretends to have inoculated 20,000 persons," someone is grossly exaggerating. From Tronchin, who was not given to writing, we have no direct expression, but Roux, an eye-witness, gives (1765) a most interesting description of the whole method of treatment as carried out in the house Tronchin had hired for the purpose of receiving his patients for inoculation. They were "prepared" for it by a dietetic régime of one month. In the particular case cited by Roux 26 days were required from the time of inoculation to the final discharge, and 10 more for the healing of the wound. There were some rather alarming symptoms in this case and de l'Epine, referring to it later, thinks it was as bad as the real smallpox, but Tronchin, in a letter to Morel (1767), says that the patients treated by his

⁸⁸ Jean-Baptiste Sézac, 1693-1770.

⁸⁹ H. Tronchin: *Un médecin du XVIII siècle*, Theodore Tronchin (1709-1781), Paris, 1906, Plon 8°. See also F. C. Shattuck in *Boston Med. and Surg. J.*, 1908, CLIX, 1-5. A less favorable judgment of Tronchin is to be found in a paper by A. Geyl, based on Dutch documents (*Arch. f. Gesch. d. Med.*, 1908, 1, 81, *et seq.*).

method in Paris were less ill than those treated by the old [79] method.⁹⁰ One really cannot wonder that people did not take to the old method and greeted the coming of Gatti a few

⁹⁰ This case of Tronchin's as reported by Roux (1765) offers so good an illustration of the method as then practised, that an extract may prove interesting: The patient is the son of d'Héricourt (*intendant de la marine*), 12 years old, delicate, anemic.

13. March 1756 régime begins, one-half of ordinary diet, chiefly farinaceous, some veal, mutton, chicken and vegetables. Every night tepid foot bath for one-half hour.

10. April. Roux moves with the young man, his pupil since 6 years, to Tronchin's house, where they sleep together in same alcove.

11. April. Surgeon Saint-Martin applies vesicant to insides of both legs.

12. April. *Inoculation:* Blisters are opened, threads with virus applied.

13. April. Removal of threads, bandage with digestive ointment, continued next day.

18. April. Around each wound red circle, beginning excavation.

20. April. Patient uneasy, headache, inguinal glands swell. Up to here from day of inoculation only vegetables, soup and barley water allowed.

21. April. Glands sensitive and painful, *fever sets in* 9 a. m. slight.

22. April. Fever higher, at 7 p. m. slight delirium, all night and next day, papules on chest.

23. April. Slight delirium and fever until 7 p. m. In morning slight epistaxis. During this febrile and eruptive period only barley water allowed.

24. April. No fever, eruption finished, slight nose-bleed.

25. April. Papules grow in size rapidly, some paler. Sixty-six on face and as many on body, distinct and with red circles.

27. April. Suppuration of pustules, wounds which were almost dry and covered by brown scab, begin to suppurate abundantly.

28. April. Some pustules begin to dry up. Saint-Martin opens some to take virus on threads.

4. May. (22d day after inoculation.) Exsiccation complete. wounds discharge for 15 further days. During febrile period, diet same as before fever set in.

9. May. Slight "erysipelas" of face and around one leg, which continues for 3 to 4 days. "Patient subject to this." No fever. Roux calls this a benign case. He mentions by name seven other patients under the care of Tronchin at the same time.

[79] years later (1760). He indeed brought simplification and perhaps went too far in the opposite direction, as some of his failures seem to indicate. Gatti hails from Pisa where he held the chair of medicine at the university. He was brought [80] to Paris by his friend Baron d'Holbach ⁹¹ and inoculated his children. Well introduced, he immediately found a great following. In 1763, 1764 and 1767 he publishes his ideas and the developments and results of his method in a direct and frank manner, which contrasted favorably with the mass of other writings. He co-operates with Roux, Antoine Petit, Bordeu ⁹² and others. His *réflexions* of 1764 particularly maintain a standpoint far in advance of his time. He sets out with a discussion of the etiology of smallpox. He objects to the lax conceptions then prevalent, expressed in vague terms of fermentation, ebullition, effervescence, humors, leaven, germ, etc. They mean nothing. Variola is always produced by the action of a foreign body introduced into the organism from the outside, by contagion or other communication. It is the constant and determinate effect of a specific "virus," which reproduces itself and multiplies. He insists especially on the specificity. Communication of the disease takes place through contact, inhalation or ingestion. These were revolutionary views then, and to-day we do not know much more about variola. By inoculation, he goes on, the poison is conveyed by intelligence, in the natural disease by chance. A preparation of a subject for inoculation has sense only if it tends to improve his general health; debilitating measures like bleeding and purging, as practised by routine even on feeble individuals, have sometimes brought tears of pity and indignation to his eyes. As to the choice of the virus it is of lesser moment whether it is "crude" or "mature"; the important factor is that the individual from whom it is derived be in good general health and free from other con-

⁹¹ P.-H.-T. d'Holbach, 1723-1789, of German origin, but settled in Paris. He achieved some fame as a sceptic philosopher and entertained at his table all the *bels esprits* of the day. Galiani called him the *premier maître d'hôtel de la philosophie*.

⁹² Théophile de Bordeu, 1722-1776.

tagious disease.⁹³ It is best to obtain the virus from another [80] inoculation and he replies to the objection made, that the virus becomes hereby weakened: "There would be nothing left to desire in the art of inoculation, if we could arrive at attenuating the variolous virus, but I do not know any means by which this attenuation can be accomplished."⁹⁴ The passage of the virus through several organisms may in time bring about a marked decrease of virulence and he adds prophetically: "Perhaps one day we may become indebted to inoculation for having brought about an attenuation of this poison among men." It is of no advantage to try and produce an abundant crop of pustules, one well developed pustule has as much protective value as a thousand. In case of doubt re-inoculation ought to be resorted to. With great vehemence Gatti turns against the unscrupulous practitioners, who, for selfish reasons, surround the method with all sorts of complicated details; he proclaims it a very simple operation and its chief principles are a thorough knowledge of the patient's condition and the art not to do harm, *partie la plus fine et la plus importante de la médecine*. He believes also that women could be instructed to the best advantage in the practice of inoculation. Gatti is absolutely convinced of the protective power of inoculated smallpox. He even substantiates this belief later by offering a considerable money prize for any authenticated case of re-infection after inoculation. Such cases, he thinks, can only happen when the eruption after inoculation is not one of true smallpox but is mistaken for it (he alludes here to chickenpox). He admits to have been deceived himself. The celebrated case of the Duchesse de Boufflers, illustrating such an instance, hurt Gatti's cause more than any other.⁹⁵

⁹³ Gatti admits that other diseases than variola can be conveyed by inoculation; it has happened to him with scarlatina and measles. Consumption (*pulmonie*) he does not believe to be thus transferred.

⁹⁴ "Je suis persuadé qu'il serait utile de pouvoir affaiblir la matière variolique, qu'il ne resterait plus rien à désirer dans l'art d'inoculer, si on pouvait y parvenir, mais que je ne connais aucun moyen d'obtenir cet affaiblissement."

⁹⁵ In the *Gaz. littér. de l'Europe*, Tome VI, p. 377 (also *Gent. Magaz. Nov.*, 1765) is given a statement of the case by the Duchesse

[80] After a careful consideration of Gatti's work and its proper [81] position in historical sequence, one is forced to the conclusion that the reformation which took place in the practice of inoculation during the sixties issued from him and that the success of Daniel Sutton and his followers is based on the methods advocated by Gatti. On the other hand it is evident that Gatti later on adopted some of the features of the Suttonian régime, notably the cold water applications and the open-air life. His adoption of the use of cold water is no blind imitation; it was based on the observation that whenever the fever, which usually follows the local eruption after three days, is delayed, the symptoms of the disease are lighter. By cold water applications he was able to delay the fever until the sixth day. But he makes no sweeping conclusions, he insists on further experiments and particularly on watching the relation of the local and general reaction.

The serious objection against inoculation, that of increasing the spread of the disease, Gatti frankly admits, but he believes that, since each infective focus is known, proper isolation could obviate any real danger. He seems, however, not to have been able to control all of his patients. That some of them had been seen to mix unhindered with others in public places was one of the chief causes of government interference. In a decree of Parliament, dated June 8, the General of Police alludes to the "murmurs of the Public" at the indiscretion of certain partisans of the method, which have "reached our ears." The "general cry" raised against the inoculators makes necessary an investigation by the enlightened magistrates. The *avocat du Roi*, Omer Joly de Fleury, then further enlarges on these reasons and concludes his address to the magistrates: "The fact of inoculation which now must fix your attention, presents itself naturally from two points of view, first as regards the principles of religion, secondly as regards the advantages humanity

de Boufflers herself. It is widely discussed in France by de l'Epine, Ant. Petit and de Baux during the deliberations of the Faculty of Medicine. The best English account, with Gatti's explanations, is to be found in Langton, *op. cit.*, pp. 18-25. (Creighton gives an abstract in his book, II, 495.)

may derive therefrom." Experts in conscience and health will [81] therefore have to be consulted. These of course are the Faculties of Theology and of Medicine respectively. The medical faculty is to give its advice first and then submit it to the theologians. The question of a continuation of a provisional tolerance to further "free literary discussion and various experiments" is set aside and it is decided to substitute for it a provisional prohibition against inoculating within the precincts of cities and suburbs until the named faculties have been able to recommend the permission, or prohibition, or tolerance of the practice.

From now on all inoculations have to be done outside the *barrières* and we see many go there, for the legally imposed limit of six weeks, to submit to inoculation. We know of numerous inoculations being performed under these restrictions by Gatti, Petit, Roux and others. Tronchin also sets up an establishment there in 1766 and Worlock,⁹⁶ the father-in-law of Sutton, and an assistant do the same.

Meanwhile the Faculty of Medicine goes to work on its report. A commission of twelve members is appointed and the procedure of investigation is outlined. This same faculty which long ago had approved, then condemned antimony, and rejected the discovery of the circulation, proposes to decide this question again on similar evidence. Not the slightest effort is made to adduce further experiments, only the literature is to be studied and the opinions which inoculators outside of Paris are asked to express. Regular meetings are held by the commission, partly in camera, partly before the assembled faculty, and tumultuous scenes occur in which parliamentary methods are forgotten and personal encounters are threatened. The commissioners soon found they could not agree and decided to present two reports instead of one. Two groups of six each were formed, one, of those in favor, led by Petit, the other, of those against inoculation, headed by de l'Epine.⁹⁷ The former represented the younger, more pro-

⁹⁶ Gardane, *Secret des Suttons*.

⁹⁷ The other commissioners in favor of inoculation with Antoine Petit were E. L. Geoffroy, A. C. Lorry, Maloët, Thiery and Cochu, while the opponents under G. J. de l'Epine's lead were, Jean Astruc, M. P. Bouvart, Th. Baron, J. Verdelhan de Miles and H. J. Mocquart.

[81] gressive, the latter the older, conservative elements. Only 15 months after the parliamentary decree could the reports be presented before the assembled faculty for the first reading and, after acceptance, be put into the printer's hands. The publication, however, was delayed until 1766 and supplements were added as late as 1767. The report of de l'Épine would do honor to any prosecuting attorney; as such it is a very clever presentation of the case against inoculation. It occupies 125 quarto pages, mostly filled by the bibliographic reviews of the literature in fine print.⁸⁸ The main points are that smallpox is not so dangerous a disease as is usually asserted. De Haën had treated 120 cases with only five deaths, which may be explained as due to other causes. Bad treatment is at the bottom of most deaths. Furthermore many people never get smallpox and a fatal inoculation might strike just those. One such case is enough to condemn inoculation. Much is made of one of Gatti's failures and of the Boston reports (Delahonde) of an increase of smallpox following inoculation. In conclusion an attempt is made to show that the provisional prohibition has had already a favorable influence on the general health in Paris and "one begins to breathe again. The epidemic, no longer nourished and perpetuated by this unfortunate practice, has lost much of its force and is notably diminished."⁸⁹

De l'Épine in his closing remarks suggests that the method

⁸⁸ Three separate sessions of the faculty were needed for the reading of this part of the report, viz., Oct. 20, 22 and 24, 1764.

⁸⁹ The summary of the conclusions is given in "nine incontestable truths" as follows:

1. Incertitude of conveying smallpox by inoculation, even if repeated.
2. Unsuccessful inoculation does not protect in future.
3. If successful there is no guarantee that attack will be benign.
4. If death is not issue, frequent disturbances may follow.
5. Same risks as in natural smallpox, disfigurement, etc.
6. Escape from death after inoculation insures no protection against other often more dangerous attacks.
7. Other diseases may be conveyed through inoculation.
8. Inoculated smallpox is sometimes fatal.
9. It can infect others and thus endanger society.

is perhaps not sufficiently perfected and hopes that the English [82] may succeed, then "we shall thank heaven for such a precious discovery and we shall render them due homage for the enlightenment which they have procured for us at their risk. It would be unjust for us to envy them the very legitimate advantage of enjoying the first fruits, reaped under such perilous circumstances." The inevitable advice of these six commissioners is neither to permit nor to tolerate inoculation.

Of the signers of this verdict Astruc¹⁰⁰ was undoubtedly the most famous and influential. Eighty years old and only two years before his death, it cannot be presumed, however, that he took a very active part in the composition of this report. Bouvart,¹⁰¹ another member, we can safely make responsible for several of the more extreme attacks against the inoculators. He was a violent antagonist of Tronchin's, whose book on the colic of Poitou he had tried to drown under a flood of ridicule and unjust criticism, and with Petit, the editor of the other report, he had had a quarrel about the very important question of belated childbirth.¹⁰²

The report of the other party, edited by Petit,¹⁰³ is not nearly as carefully prepared as the de l'Épine document. One feels that it is written by a busy practitioner who has little time and inclination to enter into all the subtleties introduced. He judges from what he has seen, simply brushing aside the objections. It is not nearly as convincing for the casual reader as the other, in which almost all the reports of inoculators are dexterously turned against themselves, thus exhibiting a formidable array of damaging testimony. Petit did not follow such tactics in his first report, but, seeing that he had failed to make an impression, comes out in 1766 with a second report in which he shows the malice of de l'Épine's method. He points out the "multiple errors and mistakes of all sorts" and these become evident enough when one compares them with the sources.

¹⁰⁰ Jean Astruc, 1684-1766.

¹⁰¹ M.-P. Bouvart, 1717-1787.

¹⁰² The contention was about the legitimacy of a child born after an 11½ months pregnancy and 10½ months after the death of the 76-year-old father.

¹⁰³ Antoine Petit. 1718-1794.

[82] This second report is signed by only three of the commissioners besides Petit, viz., Geoffroy, Lorry and Maloët,¹⁰⁴ the other two are absent and the Doyen Belleteste and the censor Le Thieullier therefore sign in their stead.

The endless discussions¹⁰⁵ about the merits of inoculation during these several years must have exhausted the interest in the subject and indeed, after the assembled faculty had expressed itself in favor of the tolerance of inoculation under certain restrictions by 52 votes against 26, we hear little more on the subject. Petit, in a later letter to the Doyen of the Faculty, thinks that, up to the end of 1766, probably 15,000 inoculations had been performed in France, which seems little against the 200,000 reported from England. Although the acuteness of popular interest¹⁰⁶ had subsided, we have good reason to assume that inoculation was continued in Paris and the provinces on a much larger scale. We have, however, no evidence that anything was done, as in England, to further study and develop the method.¹⁰⁷ We should naturally expect to hear of Gatti's further work, but there is very little to be found about him. In 1769 he receives permission to inoculate in the military college, but of his results and the details of his work I have been unable to detect traces. Louis XV dies of smallpox in 1774 and this event decides his grandson and successor, Louis XVI, to submit himself as well as his family to inoculation. Neither with Louis XV's illness nor with this inoculation do we find Gatti's name connected, although he

¹⁰⁴ Etienne-Louis Geoffroy, 1725-1810, for 40 years one of the most prominent Paris physicians; Anne-Charles Lorry 1726-1786, good observer and medical historian of merit; P. L. Maloët, 1730-1810, able practitioner.

¹⁰⁵ Dubourg, *op. cit.*

¹⁰⁶ John Wilkes during his exile in Paris seems to have become interested in inoculation to the extent of writing a farce about it (*op. cit.*).

¹⁰⁷ The principal clinical reports of this time, besides the ones already cited, are those of Robert, Rast, Grassot, Rasoux, Dezoteux, Le Camus, Gardane, Gandoher de Foigny, Mangin, Vernage (*op. cit.*). Théophile de Bordeu, the founder of the theory of "vitalism" publishes (*op. cit.*), in defence of inoculation, a long historical treatise, in which he analyses what attitude the founders of all the medical doctrines since Hippocrates might have assumed in regard to inoculation.

was physician extraordinary to the King.¹⁰⁸ Gatti's appearance and activity marks the greatest advance in variolation which was reached in France and, as a matter of fact, anywhere. His ideas and methods were those of the best scientists at the end of the 19th century and it is indeed remarkable how little his work is remembered.¹⁰⁹

In England, and to some extent also on the Continent, after the technical principles of variolation became fairly well understood, we can see developing round it a social movement for the eradication of smallpox very similar to the tuberculosis crusade of our days. I have already alluded to the hygienic features in the regimen; they were enlarged upon and generalized for a wider application. Segregation of the infected cases was insisted upon more strongly than before. Early inoculation of infants was advocated by Maty and more emphatically by Lettsom. The demands for inoculation dispensaries became very loud and several were established (John Clark at Newcastle, Haygarth at Chester, etc.). The number of inoculations practised was exceedingly great. It went to many thousands per year. We have, of course, no accurate reports about it. But already in 1766 (Houlton) we hear that Robert Sutton had inoculated 2514 persons from 1757 to [83] 1767 and Daniel 13,792 from 1764 to 1766 and his assistants 6000 more.¹¹⁰ As late as 1821 to 1822 John Forbes tells us that a farmer, Pearce and son, of Busham (Sussex) associated with some surgeons inoculated 13,000 persons!

Jenner's (born in 1749) interest in the subject dates from

¹⁰⁸ Report by de Lassone (*op. cit.*).

¹⁰⁹ In his own country, Italy, he does not seem to have exerted any great influence in favor of variolation. The considerable development which it reached there was inspired chiefly from France, Switzerland and Austria. The personal initiative of the Marchese Bufalini in Rome in 1754, the opposition of the Papal physician, Zanettini, and of Dr. Roncalli Parolino, and Tronchin's inoculation of a Bourbon prince in Parma are the main events of the Italian history of variolation. The most active Italian inoculators were Peverini, Lunadei, Lavizzari, Caluri, Targione, Manetti, Berzi, Bicetti (*op. cit.*). In Spain there seems to have been only a literary reflex of the French efforts.

¹¹⁰ His income for 1764 is given as £2200 and for 1765 as £6300.

[83] this period. John Hunter had told him already not to speculate but to observe and prove. With his natural gifts, with the inspiration of that particular period and the opportunities of his home surroundings it was inevitable that he should make the greatest improvement in the method of inoculation.

In following variolation on its course through the civilized world of the 18th century and, in noting the successive steps of its evolution, it has been my aim rather to open avenues for future research than to give a complete and detailed account of the more important phases. Plentiful suggestions are to be found everywhere which lead one to infer that variolation, without the advent of vaccination, might have furnished the world with an equally safe and perhaps more efficient method of preventive immunization. We have every reason, however, to be satisfied with the results of vaccination. Thanks to it smallpox has been practically stricken off the list of the great medical problems. None the less it is time that the epoch which preceded vaccination should receive its proper place in the history of medicine, and that the names of Kirkpatrick, Gatti, Watson, Mudge and Dimsdale should be recalled with that of Edward Jenner.

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[NOTE.—In these lists, English, German, French or other translations are indicated by E., G., F., . . . respectively, with dates. The American tracts and pamphlets of the eighteenth century are subjoined as "Americana." Certain of these which have been brought to light and identified in Professor Kittredge's interesting paper, "Some Lost Works of Cotton Mather" [Proc. Mass. Histor. Soc., Feb. 1912, pp. 418-479], are marked "K." A star (*) denotes an inaugural dissertation or thesis.]

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